

CLAIMS

1) A gamma subunit of a vertebrate AMP-activated kinase (AMPK), wherein said gamma subunit is a polypeptide comprising at least a sequence having at
5 least 70% identity with the polypeptide SEQ ID NO: 2.

2) A polypeptide of claim 1, wherein said polypeptide comprises a sequence having at least 95% identity with the polypeptide SEQ ID NO:2.

3) A polypeptide of claim 1, wherein said
10 polypeptide comprises a sequence having at least 75% identity with the polypeptide SEQ ID NO: 28.

4) A polypeptide of any of claims 1 to 3, wherein said polypeptide comprises the sequence SEQ ID NO: 2 or SEQ ID NO:4.

15 5) A polypeptide of claim 4, wherein said polypeptide comprises the sequence SEQ ID NO: 28, SEQ ID NO: 30 or SEQ ID NO: 32.

6) A polypeptide which is a functionally altered mutant of a gamma subunit of a vertebrate AMP-
20 activated kinase, wherein said polypeptide has at least a mutation located within the first CBS domain of said gamma subunit.

7) A polypeptide of claim 6, wherein the mutation is located within the region of the first CBS
25 domain aligned with the region of a polypeptide of SEQ ID NO: 2 spanning from residue 30 to residue 50.

8) A polypeptide of claim 7, wherein the mutation is a R→Q substitution or a V→I substitution.

9) A polypeptide of claim 8 selected among:
30 - a polypeptide having a sequence resulting from a R→Q substitution at a position corresponding to position 41 in SEQ ID NO: 2;

- a polypeptide having a sequence resulting from a V→I substitution at the position corresponding to
35 position 40 of SEQ ID NO: 2.

10) A polypeptide which is a mutant of a gamma subunit of a vertebrate AMP-activated kinase, wherein said polypeptide results from a deletion of a part of a polypeptide of any of claims 1 to 5.

5 11) A nucleic acid sequence encoding a polypeptide of any of claims 1 to 10, or the complement thereof, provided that said nucleic acid sequence does not consist of the EST GENBANK AA178898, or of the EST W94830.

10 12) A nucleic acid sequence of claim 11, having the sequence SEQ ID NO: 1, SEQ ID NO:3, SEQ ID NO: 27, SEQ ID NO: 29, SEQ ID NO: 31, or the complement thereof.

15 13) A nucleic acid sequence comprising at least a portion of a nucleic acid sequence encoding a polypeptide of any of claims 1 to 10, and up to 500 kb of a 3' and/or of a 5' adjacent genomic DNA sequence, or the complement thereof.

20 14) A nucleic acid fragment selected among:
- a specific fragment of a nucleic acid sequence encoding a polypeptide of any of claims 1 to 10, or of a nucleic acid sequence of claim 13;
- a nucleic acid fragment which specifically hybridises under stringent conditions with a nucleic acid sequence
25 encoding a polypeptide of any of claims 1 to 8, or of a nucleic acid sequence of claim 11;
provided that said nucleic acid fragment does not consist of the EST GENBANK AA178898 or of the EST GENBANK W94830.

30 15) A set of primers for amplifying a nucleic acid sequence of any of claims 11 to 13 or a portion thereof, comprising at least a primer consisting of a nucleic acid fragment of claim 14.

35 16) A recombinant vector comprising a nucleic acid sequence encoding a polypeptide of any of claims 1 to 10.

17) An host cell transformed by a nucleic acid sequence encoding a polypeptide of any of claims 1 to 10.

18) A transgenic animal transformed by a nucleic acid sequence encoding a polypeptide of any of
5 claims 1 to 10.

19) A knockout animal, wherein the gene encoding a polypeptide of any of claims 1 to 5 is inactive.

20) A heterotrimeric AMPK wherein the γ subunit consists of a polypeptide of any of claims 1 to
10 10.

21) A method of detecting a metabolic disorder resulting from a mutation in a gene encoding a γ subunit of AMPK, wherein said process comprises:

15 - obtaining a nucleic acid sample from a vertebrate;

- checking the presence in said nucleic acid of a nucleic acid sequence encoding a polypeptide of any of claims 1 to 10, wherein said polypeptide is
20 functionally altered.

22) A method of claim 21 wherein the disorder is correlated with an altered glycogen accumulation in the muscular cells and results from the expression of a functionally altered allele of a polypeptide of any of
25 claims 1 to 5.

23) A method of any of claims 21 or 22 wherein the presence of the nucleic acid sequence encoding said mutant polypeptide is checked by contacting said nucleic acid sample with a nucleic acid probe obtained from a
30 nucleic acid of claim 14 and spanning said mutation, under conditions of specific hybridisation between said probe and the mutant sequence to be detected, and detecting the hybridisation complex.

24) A method for obtaining a pair of primers
35 allowing to detect a genetic polymorphic marker linked to

a nucleic acid sequence encoding a polypeptide of any of claims 1 to 5, wherein said process comprises:

- screening a genomic DNA library from a vertebrate with a probe specific for a nucleic acid sequence encoding a polypeptide of any of claims 1 to 5, in order to select clones comprising said nucleic acid sequence and flanking chromosomal sequences;
- identifying a polymorphic locus in said flanking chromosomal sequences, and sequencing a DNA segment comprising said polymorphic locus ;
- designing primer pairs flanking said polymorphic locus.

25) A method of claim 24 wherein the selected clones comprise at least a portion of a nucleic acid sequence encoding a polypeptide of any of claims 1 to 5, and up to 500 kb of a 3' and/or of a 5' adjacent sequence.

26) A method of any of claims 21 to 25 wherein the vertebrate is a mammal.

27) A method of claim 26 wherein said mammal is a pig.

28) A pair of primers obtainable by the process of any of claims 24 to 26.

29) A process for detecting a dysfunction of carbohydrate metabolism resulting from the expression of a functionally altered allele of a polypeptide of any of claims 1 to 5 in a vertebrate, wherein said process comprises:

- obtaining a sample of genomic DNA from said vertebrate;
- contacting said DNA with a pair of primers of claim 28 under conditions allowing PCR amplification;
- analysing the PCR product to detect if an allele of a polymorphic marker linked to a nucleic acid sequence encoding a functionally altered allele of a polypeptide of any of claims 1 to 5 is present.

30) A process of claim 29, wherein said functionally altered polypeptide results from a R41Q substitution in SEQ ID NO: 2.

31) A process of any of claims 29 or 30,
5 wherein said vertebrate is a mammal.

32) A process of claim 31 wherein said mammal is a pig.

33) A process of claim 32 wherein the pair of primers is selected among:

10 - a pair of primers consisting of SEQ ID NO: 5 and SEQ ID NO: 6;

- a pair of primers consisting of SEQ ID NO: 7 and SEQ ID NO: 8;

15 - a pair of primers consisting of SEQ ID NO: 9 and SEQ ID NO: 10;

- a pair of primers consisting of SEQ ID NO: 11 and SEQ ID NO: 12;

- a pair of primers consisting of SEQ ID NO: 13 and SEQ ID NO: 14;

20 - a pair of primers consisting of SEQ ID NO: 15 and SEQ ID NO: 16;

- a pair of primers consisting of SEQ ID NO: 17 and SEQ ID NO: 18;

25 - a pair of primers consisting of SEQ ID NO: 19 and SEQ ID NO: 20;

- a pair of primers consisting of SEQ ID NO: 21 and SEQ ID NO: 22;

- a pair of primers consisting of SEQ ID NO: 23 and SEQ ID NO: 24;

30 - a pair of primers consisting of SEQ ID NO: 25 and SEQ ID NO: 26.

34) Use of a transformed cell of claim 17 to screen compounds able to modulate AMPK activity.

35) Use of a transgenic animal of claim 18 to
35 screen compounds able to modulate AMPK activity.

36) Use of a knockout animal of claim 19 to screen compounds able to modulate energy metabolism in the absence of a functional polypeptide of any of claims 1 to 5.

5 37) Use of an heterotrimeric AMPK of claim 20 to screen compounds able to modulate AMPK activity.